Second, the Examiner's proposed approach is explicitly disapproved of at M.P.E.P. §704.01, which reads in relevant part:

> PREVIOUS EXAMINER'S SEARCH
>
> When an examiner is assigned to act on an application which has received one or more actions by some other examiner, full faith and credit should be given to the search and action of the previous examiner unless there is a clear error in the previous action or knowledge of other prior art. In general the second examiner should not take an entirely new approach to the application or attempt to reorient the point of view of the previous examiner, or make a new search in the mere hope of finding something.

The previous Examiner issued two substantive Office Actions in which the claims were thoroughly examined in view of the prior art and 35 U.S.C. §112, resulting in most the claims being allowed. M.P.E.P. §704.01 states that the current Examiner should give "full faith and credit" to the previous Examiner's work rather than "tak[ing] an entirely new approach to the application," which seems to be what the current Examiner is proposing.

Third, such a piecemeal approach is particularly inappropriate in this application. More than two years elapsed between the Applicant's last response and the current Office Action (containing only a restriction requirement). This long delay was the result of the application being lost by U.S. Patent and Trademark Office. It is extremely unfair that now, after such a long delay that was not the Applicant's fault, after the application had been given a thorough examination and most claims allowed, the Applicant should find himself back at square one.

Despite being unhappy with her proposed course of action, the Applicant sincerely thanks the current Examiner for her apology on behalf of the U.S. Patent and Trademark Office for the lengthy interval of time that elapsed between the Applicant's response on February 28, 2001 and the current Office Action, an interval in which the application was misplaced by the U.S. Patent and Trademark Office. The interval that elapsed was in no way the current Examiner's fault and the Applicant thanks the current Examiner for her diligent efforts to locate the application.

The Applicant notes that in the Office Action dated November 30, 2000, the previous Examiner returned a copy of the Form 1449 that had been submitted with the Information Disclosure Statement filed September 12, 2000. The previous Examiner placed his initials next to each entry on the Form 1449 except one: Upcroft P., et al. Rapid and efficient method for cloning of blunt-ended DNA fragments. Gene. 1987;51(1):69-75. No explanation for this omission was given in the Office Action. The Applicant requests that the current Examiner consider Upcroft P., et al. Rapid and efficient method for cloning of blunt-ended DNA fragments. Gene. 1987;51(1):69-75. For the convenience of the current Examiner, the Applicant has enclosed a copy of Upcroft P., et al. Rapid and efficient method for cloning of blunt-ended DNA fragments. Gene. 1987;51(1):69-75 and a copy of the Form 1449. The Applicant requests that the current Examiner return a copy of the Form 1449 with her initials next to the entry for Upcroft P., et al. Rapid and efficient method for cloning of blunt-ended DNA fragments. Gene. 1987;51(1):69-75 after the current Examiner has considered this publication.

**THE RESTRICTION REQUIREMENT**

The Examiner required restriction to one of the following groups:

Group I – Claims 1-30, drawn to methods of inserting a nucleic acid fragment into a circular vector;

Group II – Claims 33-36 and 65, drawn to a mixture of nucleic acid vectors;

Group III – Claims 37-38, 40-41, 54-55, 60-61, and 66, drawn to nucleic acid inserts, kits, vectors and libraries wherein the nucleic acids comprise cohesive ends which cannot be covalently joined by ligase;

Group IV – Claims 42-47, 51-52, and 57-58, drawn to nucleic acid inserts, kits, vectors and libraries wherein the nucleic acids comprise an end linked to a topoisomerase;

Group V – Claims 48-50, drawn to a nucleic acid insert and kit comprising a cos site;

Group VI – Claims 53, 56, 59, and 62, drawn to a nucleic acid insert, construct, and libraries, wherein the insert does not comprise a cos site;

Group VII – Claims 63-64, drawn to libraries of nucleic acid vectors without an insert size bias; and

Group VIII – Claims 67-68, drawn to methods for insertion of a nucleic acid into a circular vector.

The Applicants elect, without traverse, Group I, claims 1-30.

The time for responding to the Office Action was set for April 13, 2003. Enclosed herewith is a Petition for the Extension of Time under 37 C.F.R. § 1.136(a) for a period sufficient to permit the filing of this response.

The Applicants hereby also make a Conditional Petition for any relief available to correct any defect seen in connection with this filing, or any defect seen to be remaining in this application after this filing. The Commissioner is authorized to charge Kenyon & Kenyon's Deposit Account No. 11-0600 for the Petition fee and any other fees required to effect this Conditional Petition.

Respectfully submitted,

Date: May 13, 2003

Joseph A. Coppola
Reg. No. 38,413
Attorney for Applicants
KENYON & KENYON
One Broadway
New York, NY 10004
(212) 425-7200 (telephone)
(212) 425-5288 (facsimile)

| INFORMATION DISCLOSURE STATEMENT BY APPLICANTS | ATTY. DOCKET NO. 11639/1 | SERIAL NO. 09/213,834 |
|---|---|---|
| | APPLICANT(S) Y. Romantchikov | |
| | FILING DATE December 17, 1998 | GROUP 1631 |

#15

RECEIVED
MAY 18 2003
TECH CENTER 1600/2900

SEP 14 2000 PATENT & TRADEMARK OFFICE

OIPE MAY 15 2003 PATENT & TRADEMARK OFFICE

**U. S. PATENT DOCUMENTS**

| EXAMINER INITIAL | PATENT NUMBER | PATENT DATE (MM/DD/YY) | NAME | CLASS | SUBCLASS | FILING DATE |
|---|---|---|---|---|---|---|
| | | | | | | |
| | | | | | | |

**FOREIGN PATENT DOCUMENTS**

| EXAMINER INITIAL | DOCUMENT NUMBER | DATE (MM/DD/YY) | COUNTRY | CLASS | SUBCLASS | TRANSLATION YES | TRANSLATION NO |
|---|---|---|---|---|---|---|---|
| | | | | | | | |

**OTHER DOCUMENTS**

| EXAMINER INITIAL | | AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC. |
|---|---|---|
| | | Aslanidis C, et al. Ligation-independent cloning of PCR products (LIC-PCR). Nucleic Acids Res. 1990 Oct 25;18(20):6069-74. |
| | | Bercovich JA, et al. Effect of DNA concentration on recombinant plasmid recovery after blunt-end ligation. Biotechniques. 1992 Feb;12(2):190, 192-3. |
| | | Boyd AC. Turbo cloning: a fast, efficient method for cloning PCR products and other blunt-ended DNA fragments into plasmids. Nucleic Acids Res. 1993 Feb 25;21(4):817-21 |
| | | Damak S, et al. A simple two-step method for efficient blunt-end ligation of DNA fragments. Biotechniques. 1993 Sep;15(3):448-50, 452. |
| | | Mead DA, et al. A universal method for the direct cloning of PCR amplified nucleic acid. Biotechnology (N Y). 1991 Jul;9(7):657-63. |
| | | Nisson PE, et al. Rapid and efficient cloning of Alu-PCR products using uracil DNA glycosylase. PCR Methods Appl. 1991 Nov;1(2):120-3. |
| | | Pecenka V, et al. Simple and efficient method for cloning of large DNA fragments with identical ends into plasmid vectors. Nucleic Acids Res. 1988 May 11;16(9):4179. |
| | | Rashtchian A, et al. Uracil DNA glycosylase-mediated cloning of polymerase chain reaction-amplified DNA: application to genomic and cDNA cloning. Anal Biochem. 1992 Oct;206(1):91-7. |
| | | Revie D, et al. Kinetic analysis for optimization of DNA ligation reactions. Nucleic Acids Res. 1988 Nov 11;16(21):10301-21. |

| EXAMINER INITIAL | | AUTHOR, TITLE, DATE, PERTINENT P[redacted]S, ETC. |
|---|---|---|
| | | Sekiguchi J, et al. Covalent DNA binding by vaccinia topoisomerase results in unpairing of the thymine base 5' of the scissile bond. J Biol Chem. 1996 Aug 9;271(32):19436-42. |
| | | Sekiguchi J, et al. Identification of contacts between topoisomerase I and its target DNA by site-specific photocrosslinking. EMBO J. 1996 Jul 1;15(13):3448-57 |
| | | Sekiguchi J, et al. Vaccinia topoisomerase binds circumferentially to DNA. J Biol Chem. 1994 Dec 16;269(50):31731-4. |
| | | Shuman S. Novel approach to molecular cloning and polynucleotide synthesis using vaccinia DNA topoisomerase. J Biol Chem. 1994 Dec 23;269(51):32678-84. |
| | | Shuman S, et al. Site-specific interaction of vaccinia virus topoisomerase I with base and sugar moieties in duplex DNA. J Biol Chem. 1993 Sep 5;268(25):18943-50. |
| | | Shuman S. Two classes of DNA end-joining reactions catalyzed by vaccinia topoisomerase I. J Biol Chem. 1992 Aug 25;267(24):16755-8. |
| | | Shuman S. Site-specific interaction of vaccinia virus topoisomerase I with duplex DNA. Minimal DNA substrate for strand cleavage in vitro. J Biol Chem. 1991 Jun 15;266(17):11372-9. |
| | | Upcroft P, et al. Rapid and efficient method for cloning of blunt-ended DNA fragments. Gene. 1987;51(1):69-75. |
| | | Aguan K, Kusano T, Suzuki N, Kitagawa Y.<br>An improved method for the construction of high efficiency cDNA library in plasmid or lambda vector.<br>Nucleic Acids Res. 1990 Feb 25;18(4):1071. |
| | | Alexander DC, McKnight TD, Williams BG.<br>A simplified and efficient vector-primer cDNA cloning system.<br>Gene. 1984 Nov;31(1-3):79-89. |
| | | Andersson B, Wentland MA, Ricafrente JY, Liu W, Gibbs RA.<br>A "double adaptor" method for improved shotgun library construction.<br>Anal Biochem. 1996 Apr 5;236(1):107-13. |
| | | Bellemare G, Potvin C, Simard C, Larouche L.<br>Use of a phage vector for rapid synthesis and cloning of single-stranded cDNA.<br>Gene. 1987;52(1):11-9. |
| | | Bellemare G, Potvin C, Bergeron D.<br>High-yield method for directional cDNA library construction.<br>Gene. 1991 Feb 15;98(2):231-5. |
| | | Boel E, Hjorth AL, Moller KB, Moller PH.<br>A short synthetic adaptor as second-strand primer in the construction of cDNA libraries by the vector-primer method.<br>Biotechniques. 1991 Jul;11(1):26, 28. |
| | | Bottger EC.<br>An adaptor strategy to subclone entire cDNA libraries as single insert recombinants.<br>Biotechniques. 1989 Oct;7(9):925-6, 928-9. |
| | | Carninci P, Hayashizaki Y.<br>High-efficiency full-length cDNA cloning.<br>Methods Enzymol. 1999;303:19-44. |
| | | Coleclough C, Erlitz FL.<br>Use of primer-restriction-end adapters in a novel cDNA cloning strategy.<br>Gene. 1985;34(2-3):305-14. |

| EXAMINER INITIAL | | AUTHOR, TITLE, DATE, PER[illegible]NT P[illegible]S, ETC. |
|---|---|---|
| | | Collins J, Brüning H. Plasmids Useable As Gene-Clonong Vectors In An In Vitro Packaging By Coliphage: Cosmids. Gene. 1978; 4:305-14. |
| | | Edwards et al., Oligodesxyribonucleotide litigation to single-stranded cDNA: a new tool for cloning 5'ends of mRNAs and for constructing cDNA libraries by in vitro amplification, Nucleic Acids Research, 1991 19(19): 5227-32. |
| | | Gubler U, Hoffman BJ.<br>A simple and very efficient method for generating cDNA libraries.<br>Gene. 1983 Nov;25(2-3):263-9. |
| | | Haun RS, Serventi IM, Moss J.<br>Rapid, reliable ligation-independent cloning of PCR products using modified plasmid vectors.<br>Biotechniques. 1992 Oct;13(4):515-8. |
| | | Haymerle H, Herz J, Bressan GM, Frank R, Stanley KK.<br>Efficient construction of cDNA libraries in plasmid expression vectors using an adaptor strategy.<br>Nucleic Acids Res. 1986 Nov 11;14(21):8615-24. |
| | | Heidecker G, Messing J.<br>Sequence analysis of zein cDNAs obtained by an efficient mRNA cloning method.<br>Nucleic Acids Res. 1983 Jul 25;11(14):4891-906. |
| | | Hu WN, Kopachik W, Band RN.<br>A simple, efficient method to create a cDNA library.<br>Biotechniques. 1992 Dec;13(6):862-4. |
| | | Land H, Grez M, Hauser H, Lindenmaier W, Schutz G.<br>5'-Terminal sequences of eucaryotic mRNA can be cloned with high efficiency.<br>Nucleic Acids Res. 1981 May 25;9(10):2251-66. |
| | | Lang KM, Spritz RA.<br>Cloning specific complete polyadenylylated 3'-terminal cDNA segments.<br>Gene. 1985;33(2):191-6. |
| | | MacGillivray RT, Degen SJ, Chandra T, Woo SL, Davie EW.<br>Cloning and analysis of a cDNA coding for bovine prothrombin.<br>Proc Natl Acad Sci U S A. 1980 Sep;77(9):5153-7. |
| | | Norgard MV, Tocci MJ, Monahan JJ.<br>On the cloning of eukaryotic total poly(A)-RNA populations in Escherichia coli.<br>J Biol Chem. 1980 Aug 25;255(16):7665-72. |
| | | Okayama H, Berg P.<br>High-efficiency cloning of full-length cDNA.<br>Mol Cell Biol. 1982 Feb;2(2):161-70. |
| | | Okayama H, Berg P.<br>Bacteriophage lambda vector for transducing a cDNA clone library into mammalian cells.<br>Mol Cell Biol. 1985 May;5(5):1136-42. |
| | | Oliner JD, Kinzler KW, Vogelstein B.<br>In vivo cloning of PCR products in E. coli.<br>Nucleic Acids Res. 1993 Nov 11;21(22):5192-7. |
| | | Petty IT, Hunter BG, Jackson AO.<br>A novel strategy for one-step cloning of full-length cDNA and its application to the genome of barley stripe mosaic virus.<br>Gene. 1988 Dec 30;74(2):423-32. |

| EXAMINER INITIAL | | AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC. |
|---|---|---|
| | | Pheiffer BH, Zimmerman SB.<br>Polymer-stimulated ligation: enhanced blunt- or cohesive-end ligation of DNA or deoxyribooligonucleotides by T4 DNA ligase in polymer solutions.<br>Nucleic Acids Res. 1983 Nov 25;11(22):7853-71. |
| | | Pruitt SC.<br>Expression vectors permitting cDNA cloning and enrichment for specific sequences by hybridization/selection.<br>Gene. 1988 Jun 15;66(1):121-34. |
| | | Rusche JR, Howard-Flanders P.<br>Hexamine cobalt chloride promotes intermolecular ligation of blunt end DNA fragments by T4 DNA ligase.<br>Nucleic Acids Res. 1985 Mar 25;13(6):1997-2008. |
| | | Sartoris S, Cohen EB, Lee JS.<br>A rapid and improved method for generating cDNA libraries in plasmid and phage lambda vectors.<br>Gene. 1987;56(2-3):301-7. |
| | | Schmid A, Cattaneo R, Billeter MA.<br>A procedure for selective full length cDNA cloning of specific RNA species.<br>Nucleic Acids Res. 1987 May 26;15(10):3987-96. |
| | | Spickofsky N, Margolskee RF.<br>A highly efficient directional cDNA cloning method utilizing an asymmetrically tailed linker-primer plasmid.<br>Nucleic Acids Res. 1991 Dec;19(25):7105-11. |
| | | Tseng H.<br>DNA cloning without restriction enzyme and ligase.<br>Biotechniques. 1999 Dec;27(6):1240-4. |





| EXAMINER | DATE CONSIDERED 10/11/01 |
|---|---|

EXAMINER: Initial if citation considered, whether or not citation is in conformance with M.P.E.P. 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

294876